Absorption of irrigation fluid occurs frequently during high power 532 nm laser vaporization of the prostate

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Abstract: Purpose Absorption of irrigation fluid was not detected during GreenLight™ laser vaporization of the prostate using the first generation 80 W laser. However, data are lacking on intraoperative irrigation fluid absorption using the second generation 120 W high power laser. We assessed whether fluid absorption occurs during high power laser vaporization of the prostate. Materials and Methods We performed this prospective investigation at a tertiary referral center in patients undergoing 120 W laser vaporization for prostatic bladder outlet obstruction. Normal saline containing 1% ethanol was used for intraoperative irrigation. The expired breath ethanol concentration was measured periodically during the operation using an alcometer. The volume of saline absorption was calculated from these concentrations. Intraoperative changes in hematological and biochemical blood parameters were also recorded. Results Of 50 investigated patients 22 (44%) had a positive breath ethanol test. Median absorption volume in the absorber group was 725 ml (range 138 to 3,452). Ten patients absorbed more than 1,000 ml. Absorbers had a smaller prostate, more capsular perforation, higher bleeding intensity and more laser energy applied during the operation. Three patients (13%) had symptoms potentially related to fluid absorption. Hemoglobin, hematocrit and serum chloride were the only blood parameters that changed significantly in the absorber group. The changes were significantly different than those in nonabsorbers. Conclusions Fluid absorption occurs frequently during high power laser vaporization of the prostate. This should be considered in patients who present with cardiopulmonary or neurological symptoms during or after the procedure.

DOI: https://doi.org/10.1016/j.juro.2014.07.117

Absorption of irrigation fluid occurs frequently during high power 532 nm laser vaporization of the prostate. Journal of Urology, 193(1):211-216.
DOI: https://doi.org/10.1016/j.juro.2014.07.117

Absorption of irrigation fluid occurs frequently during high-power 532nm laser vaporization of the prostate

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Runninghead: Fluid absorption during prostate laser vaporization

Keywords: Vaporization, laser, Intraoperative monitoring, Prostatic hyperplasia/*surgery, Intraoperative complications

ABSTRACT

Purpose: Absorption of irrigation fluid was undetectable during greenlight laser vaporization (LV) of the prostate using the first-generation 80W laser. **However, data on intraoperative irrigation fluid absorption for the second-generation 120W high power laser is lacking.** The purpose of this investigation was to assess whether fluid absorption occurs during high-power LV of the prostate.

Materials and Methods: This prospective investigation was conducted in a tertiary referral center with patients undergoing 120W LV for prostatic bladder outlet obstruction. Normal saline containing 1% ethanol was used for intraoperative irrigation. Expired breath-ethanol concentrations were measured periodically during the operation using an alcometer. The volume of saline absorption was calculated from these concentrations. Intraoperative changes in hematological and biochemical blood parameters were also recorded.

Results: Of 50 investigated patients, 22 (44%) had a positive breath-ethanol test. The median absorption volume in the absorber group was 725ml (range: 138-3452ml). Ten patients absorbed more than 1000ml. Absorbers had smaller prostates, more capsular perforations, a higher bleeding intensity, and more laser energy was applied during their operations. Three patients (13%) had symptoms potentially related to fluid absorption. Hemoglobin, hematocrit and serum chloride were the only blood parameters, which changed significantly in the absorber group and showed a significantly different change in the group of absorbers compared to non-absorbers.

Conclusions: Fluid absorption occurs frequently during high-power LV of the prostate. It should be taken into consideration in patients presenting with cardiopulmonary or neurological symptoms during or after the procedure.

Introduction

Laser vaporization (LV) of the prostate using the 532nm (green light) laser system is a minimally invasive treatment option for patients suffering from lower urinary tract symptoms secondary to prostatic bladder outlet obstruction.[1] The technique has several advantages over conventional transurethral resection of the prostate (TURP), which make the procedure particularly appealing for high-risk cardiovascular patients[2]: The coagulation properties of the laser minimize bleeding complications even in patients undergoing anticoagulation or platelet inhibition treatment.[3] Furthermore, intraoperative irrigation with isotonic saline prevents the development of a classical TUR-syndrome, which is known to be a result of excess influx of electrolyte-free glycine solution into the vascular system during transurethral surgery.[4] Finally, it is postulated that synchronous tissue coagulation during LV inhibits absorption of irrigation fluid in general.[5] Extensive absorption of irrigation fluid, even isotonic, carries the risk of cardiopulmonary complications particularly in patients with preexisting cardiovascular risk factors.[4,6]

Fluid absorption was undetectable during LV using the first generation low-power (80W) 532nm laser.[7] **However, data on irrigation fluid absorption during LV using the second-generation high-power (120W) laser is lacking.**

The aim of this investigation was to assess whether and to what extent intraoperative fluid absorption occurs during high-power LV of the prostate.

Materials and Methods

This prospective study was performed in a tertiary referral center with a consecutive series of patients undergoing routine LV of the prostate for symptomatic prostatic bladder outlet obstruction between July 2011 and August 2012. Patients with known alcoholism or liver disease were excluded from the study because the irrigation solution contained ethanol. The local ethics committee approved the study and all patients provided written informed consent.

The decision to perform a LV was based on preoperative clinical assessment as well as the co-morbidities and preferences of the patient. The preoperative assessment involved a thorough history, physical examination and specific investigations (uroflowmetry, post-void residual volume measurement, trans-rectal ultrasound of the prostate and laboratory investigations including a complete blood count, coagulation parameters, serum electrolytes, creatinine, a prostate specific antigen test, urinalysis and a urine culture). The International Prostate Symptom Score / Quality of Life questionnaire was also part of the preoperative assessment.

All operations were performed by experienced staff surgeons (n=4) or by senior residents (n=3) in form of a supervised teaching operation. The operations took place under either general anesthesia with tracheal intubation or spinal anesthesia. The 120W GreenLight HPS™ laser (American Medical Systems®, Minnetonka, USA) and a 24F continuous flow Iglesias laser resectoscope (Karl Storz GmbH, Tuttlingen, D) coupled to an automated irrigation-suction pump system (Endo Fluid Management System Urology, Future Medical Systems, Genève, CH) were used for the procedure. Vaporization was performed until the appearance of a TURP-like cavity as described earlier.[8]

The non-invasive expired breath ethanol test was used to detect and quantify intraoperative absorption of irrigation fluid.[9,10] Intraoperative irrigation was performed using isotonic saline containing 1% ethanol as a tracer for absorption (B.Braun Medical AG, Sempach, CH). At the beginning and every ten minutes throughout the procedure the end-expiratory breath ethanol concentration was measured using an AlcoQuant 6020 alcometer (EnviteC GmbH, Wismar, D) as described previously.[11] **The alcometer was connected to the endotracheal tube if patients were under general anesthesia. Patients under spinal anesthesia were asked to breathe directly into the alcometer. The alcometer was calibrated regularly as per the guidelines of the manufacturer.**

The breath ethanol concentrations were converted into blood ethanol concentrations to estimate the amount of fluid absorption during the operation using the nomogram of Hahn.[10] The surgeons were blinded to the results of the ethanol measurements, but were informed if the estimated absorption volume exceeded a critical volume of two liters. At that point the surgeons were advised to terminate the procedure expeditiously **and ethanol-free saline was used for further irrigation to minimize the risk of ethanol intoxication**.[10] For the final analyses the total absorption volumes and absorption over time were calculated using the exact mathematical formula of Hahn.[9]

Hematological (hematocrit, hemoglobin) and biochemical serum parameters (sodium, potassium, chloride) as well as the venous pH were measured prior to the operation, after 30 min and at the end of the operation to assess whether absorption causes changes in these parameters and whether the changes can be used to detect absorption. The most pronounced change from the baseline value was utilized for statistical analyses.

After the operations the surgeons were asked to report intraoperative events, which are known risk factors of fluid absorption (i.e. capsular perforation, injury to prostatic sinuses or deep bladder neck incision). Furthermore, the surgeons rated the bleeding intensity during the operation on a scale from 1 to 5 (1=no bleeding, 2=non-disturbing **bleeding**, 3=impaired visibility **due to bleeding**, 4=prolonged operation time **as a consequence of bleeding**, 5=termination of surgery **due to uncontrollable bleeding**).

Statistical analyses were performed using SPSS Statistics version 22 (IBM, Armonk, USA). Differences between the blood tests at baseline and throughout the operation were compared using the Wilcoxon signed-rank test. The Mann-Whitney U-test was utilized to compare differences in changes of these blood tests between absorbers and non-absorbers. All p-values <0.05 were considered statistically significant.

Results

A total of 50 patients were investigated in this study. Their baseline characteristics are summarized in Table 1. The median operative time was 70min (range: 30-170min) and the median applied laser energy 230kJ (65-400kJ). Experienced staff surgeons performed 36 procedures (72%). Fourteen LVs (28%) were done by senior residents as a teaching operation.

A positive ethanol breath test was detected in 22 patients (44%). In these patients the measured blood ethanol values ranged from 0.04 to 1.03mg/ml. Figure 1 illustrates the calculated volumes of absorbed irrigation fluid for each of the 22 patients. The median absorption volume in the group of absorbers was 725ml (range: 138-3452ml). Ten patients absorbed more than 1000ml, six patients had absorption volumes greater than 2000ml and one patient greater than 3000ml.

Figure 2 illustrates the temporal appearance and the duration of the positive breath tests. Fluid absorption occurred in the second half of the procedure in 16 patients (73%). In the majority of patients the measured ethanol values increased slowly (<0.25mg/ml per measurement) or remained stable over time. However, in five patients (23%) a steep increase of the ethanol values (>0.25mg/ml up to 0.89mg/ml per measurement) was detectable.

Differences between patients with and without a positive ethanol breath test are shown in Table 2. Patients with a positive test had smaller prostates but a slightly higher amount of total energy applied, a higher bleeding intensity and more intraoperative events (capsular perforation, opened venous sinuses, bladder neck incision). **Five of ten patients with fluid absorption greater than 1000ml did not have such intraoperative events.** All other investigated factors were not relevantly different between the two groups.

In the absorber group significant changes were detectable for hemoglobin (from median 12.9 to 12.1g/dl; p<0.001), hematocrit (39.5 to 37.1%; p<0.001), venous pH (7.4 to 7.34; p=0.002) and serum chloride (108 to 111mmo/l; p=0.001). Changes of serum sodium or potassium were non-significant in this group (data not shown). In the non-absorber group significant changes were detected for serum potassium (3.9 to 4.4mmol/l; p=0.02) and venous pH (7.39 to 7.37; p=0.002). The remaining blood parameters did not change significantly (data not shown).

Figure 3 illustrates the differences in changes of the investigated blood parameters between the group of absorbers and non-absorbers. Significant differences between the groups were only detectable for hemoglobin, hematocrit and serum chloride. Of note, in either group none of the parameters showed a decrease or increase exclusively. Additionally, for each parameter the general direction of the change from baseline (i.e. increase or decrease) was the same for absorbers and non-absorbers.

The majority of patients in the absorber group (n=19; 87%) remained clinically asymptomatic. However three patients (13%) had symptoms potentially related to fluid absorption. Two patients had mild dyspnea and low oxygen saturation after the operation and were treated with oxygen inhalation. Furosemide was given in one of these patients who also had a significant increase of his body weight. In one patient a venous sinus was injured during the operation and a steep increase of his ethanol concentration (from 0 to 0.89mg/ml) was detected after 80 minutes operative time. His calculated absorption volume was 2880ml. The second symptomatic patient had significant bleeding during the operation (grade 4 of 5). The ethanol concentration slowly increased from 0 to 0.46mg/ml over 40 minutes and the calculated absorption volume was 1919ml. The third patient had an indwelling catheter, a positive preoperative urine culture and was on acetylsalicylic acid medication. He underwent a bladder neck incision at the end of the procedure and a steep increase of his ethanol concentration occurred. His calculated absorption volume was 2449ml. He had a low body temperature of 35.2°C, an oxygen saturation of 94%, and neurological symptoms in form of a reduced state of consciousness (Glasgow coma scale 6 of 15) immediately after the procedure. One hour after the procedure the patient was fully awake and further investigations did not reveal any neurological deficits. He was discharged 4 days after the procedure in normal general condition.

Postoperative clot evacuations or re-operations were not necessary in any of the patients. Re-catheterization after catheter removal was required in 17 patients (34%) due to urinary retention (n=12), high residual volumes (n=3) or urinary tract infections (n=2). The median time to definitive catheter removal was 3 days (2-20 days) and the median postoperative hospital stay was 4 days (2-11 days).

Discussion

This prospective investigation revealed that absorption of irrigation fluid is a frequent event during high-power 532nm LV of the prostate. The rate of fluid absorption in our study was unexpectedly high. Almost every second patient had a positive ethanol breath test. A relevant proportion of these patients absorbed high volumes and some of them in a very short period of time. Clinical symptoms were rare and only mild to moderate and a classical TUR-syndrome was not detectable due to the use of normal saline for irrigation. However, the unperceived absorption of high volumes of saline carries the risk of fluid overload, which can become clinically significant particularly in cardiovascular high-risk patients who mainly benefit from the LV procedure.[1,2] Massive influx of isotonic saline and fluid overload can lead to pulmonary edema.[12] Additionally, hyperchloremic acidosis, reduced glomerular filtration rate, impaired myocardial function as well as abdominal pain and mental dizziness have been reported to be a result of excess saline influx.[12]

Numerous tests have been evaluated to quantify fluid absorption during transurethral surgery, but most of them have been shown to be unreliable (i.e. volumetric fluid balance or gravimetry) due to confounding factors or are rarely used due to practical problems and invasiveness (i.e. measurements of central venous pressure or isotopes).[4] Breath ethanol measurements have been extensively evaluated for different types of endoscopic procedures.[4,10] Calculations of fluid absorption from breath ethanol measurements have been optimized by taking different factors into account (i.e. type of absorption, ethanol metabolism and re-distribution) and nomograms have been developed.[10] Numerous studies have been performed to quantify fluid absorption and to identify risk factors for fluid absorption during conventional TURP.[13-16] Barber and colleagues were the first who investigated fluid absorption during 532nm LV of the prostate using the breath ethanol test.[7] They investigated 40 patients during LV with the first-generation 80W laser. The ethanol measurements remained negative throughout all procedures. The differences between their results and the results of the present investigation can be explained by the different characteristics of the two lasers. The low baseline output power (80W) of the first generation laser was accompanied by a decrease of the power output during the procedure caused by laser fiber degradation.[8] It is likely that tissue ablation deep enough to reach the prostatic capsule, was not achieved with the 80W laser. Accordingly, intraoperative bleeding and capsular perforations, which are both risk factors for fluid absorption[11,17] were rare events during 80W LV.[18-20] Increased output power (120W) and a less extensive decrease of power output during the procedure due to improved laser fibers resulted in more extensive tissue ablation but also in more bleeding complications and capsular perforations during LV using second-generation laser.[18,19,21] In the present investigation capsular perforations, opening of venous sinuses and increased bleeding intensity were found more often in the absorber group.

Our study **supports** the assumption that tissue ablation near the prostatic capsule increases the risk of fluid absorption. The majority of positive tests occurred in the second half of the operation when the procedure approaches the prostatic capsule. Furthermore, in the absorber group the prostate volume was smaller but the applied total laser energy higher, indicating a more extensive ablation. Extensive tissue ablation has been identified as a risk factor for fluid absorption during TURP.[22] In contrast, smoking, a high ASA score, anticoagulation and urinary tract infections of which some were previously identified as risk factors for fluid absorption[11,14], were not obviously associated with absorption in our investigation. It seems that the experience of the surgeon does not influence the risk of fluid absorption.

Our investigation revealed that high volumes of irrigation fluid can be absorbed in a short period of time, **without a clinically obvious vascular injury** and even under low-pressure irrigation. **The active suction mechanism of the pump used in the present study results in**

much slower filling of the bladder and a lower intravesical pressure over a longer period of time. Furthermore, maximum intravesical pressure can be predefined to minimize high-pressure peaks. It has previously been shown that low-pressure irrigation does not prevent but decreases the amount of fluid absorption during transurethral surgery.[11,23,24] Furthermore, the operations were expeditiously terminated if a critical absorption volume was measured during ethanol monitoring. Thus, it is likely that in the absence of low-pressure irrigation and ethanol monitoring higher volumes of fluid absorption and potentially a higher rate of clinical symptoms would have been detectable.

Hyponatremia, which can be used as indicator for fluid absorption if hypo-osmolar solutions are used[4] was not detectable in the present investigation because isotonic fluid was used. Hemoglobin, hematocrit and serum chloride were the only blood tests that showed both a significant decrease in the absorber group and a significantly different change in the group of absorbers compared to the non-absorbers. However, in contrast to ethanol, conventional blood parameters are also affected by the amount of fluids given intravenously and therefore are not reliable to monitor fluid absorption.[4,10]

A limitation to our study is that it was not powered to analyze potential risk factors for fluid absorption during LV of the prostate in detail. **Therefore, we did not perform statistical analyses but only exploratory analyses for this aspect. A larger study is required to formally assess these risk factors.**

Conclusions

Absorption of large volumes of irrigation fluid should be taken into consideration if patients undergoing high power 532nm LV of the prostate show cardio-pulmonary or neurological symptoms. The ethanol breath test is an easy-to-perform, non-invasive test that enables early detection of fluid absorption and thus allows a timely initiation of treatment and adequate postoperative patient care.

Acknowledgements:

The authors thank Ms. Alexandra Veloudios for the excellent organization of the patient care during this study.

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Figure legends

Figure 1:

The calculated amount of fluid absorption in each of the 22 patients with a positive ethanol breath test.

Figure 2:

Temporal appearance of the positive ethanol breath tests and their duration for the 22 patients with a positive test.

Figure 3:

Boxplots showing differences in changes of the investigated blood parameters in patients with a positive (absorber) and negative ethanol breath test (non absorber). All boxplots represent the median, interquartile range and ±1.5x interquartile range.